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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/612,829	07/07/2000	Howard Gregg King	4396D1	8746

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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 12/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/612,829	KING ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-18,20,21,23,24 and 26-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18,20,21,23,24 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 5 October 2005 does not place the application in condition for allowance.

Status of Rejections Pending Since the Office Action of 5 July 2005

2. All rejections of claims 19, 22, and 25 are obviated due to cancellation of the claims.

3. The rejections of claims 23 and 26 as obvious over Adourian et al in view of Lewis are maintained.

4. All other rejections are withdrawn due to Applicant's amendment.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 27, 29, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Adourian et al. As the application dates of the instant application and Adourian et al

are the same (14 September 1998), citations below are given to provisional application 60/058,798, to which Adourian et al claimed benefit of priority, and which was filed on 15 September 1997.

Regarding claim 27, Adourian et al disclose a method for sample handling in a capillary electrophoresis apparatus, comprising: providing a plurality of samples on coordinates of a work surface (Page 18, lines 1-15; Page 9, lines 10-15); simultaneously transferring at least two samples from their respective work-surface coordinates to respective loading wells of a capillary electrophoresis chip (Page 19, lines 17-18; Page 6, line 20 - Page 7, line 20), wherein each loading well is in fluid communication with a respective capillary formed in a monolithic substrate (e.g. Figures 8A and 8B; either loading channel 2 or separation channel 3 reads on the claimed capillary) and each capillary comprises a capillary of a multi-channel capillary electrophoresis apparatus (Figure 8B); and injecting the samples from the wells into the capillaries. (Page 19, line 9 - Page 20, line 1; Page 9, lines 10-24)

Regarding claim 29, each capillary comprises an inlet. (Figures 8A and 8B)

Regarding claim 31, for successful operation, there can be no motion between the capillary and loading well in this system. If loading channel 2 is taken to be the capillary, such motion would in fact be impossible.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 14-17, 20, 21, 23, 24, 26, 28, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al in view of Lewis. As the application dates of the instant application and Adourian et al are the same (14 September 1998), citations

below are given to provisional application 60/058,798, to which Adourian et al claimed benefit of priority, and which was filed on 15 September 1997.

Regarding claim 14, Adourian et al disclose a method for sample handling in a capillary electrophoresis apparatus, comprising: providing a plurality of samples on coordinates of a work surface (Page 18, lines 1-15; Page 9, lines 10-15); simultaneously transferring at least two samples from their respective work-surface coordinates to respective loading wells of a capillary electrophoresis chip (Page 19, lines 17-18; Page 6, line 20 - Page 7, line 20), wherein the wells include a capillary fixedly positioned therein (e.g. Figures 1A and 8A; Page 19, line 9 - Page 20, line 1; Page 9, lines 10-24); and injecting the samples from the wells into the capillaries. (Page 19, line 9 - Page 20, line 1; Page 9, lines 10-24) Applicant's definition of capillaries includes such microfluidic structures. (Specification Page 5, lines 4-8)

Regarding claim 15, Adourian et al disclose the work surfaces being multiwell plates, with the sample coordinates defined by the wells. (Page 9, lines 10-15; Page 18, lines 1-15)

Regarding claim 16, the loading wells of Adourian et al can be referred to as being in a sample loading assembly. (Figure 7, Page 8, line 26 - Page 9, line 15; the arm, pipetter head, microtiter plate and microelectrophoresis device can be referred to as a "sample loading assembly")

Regarding claim 17, Adourian et al disclose electrokinetic injection. (Page 9, lines 18-24)

Regarding claim 20, Adourian et al disclose the sample well being a well of a conventional 96-well microtiter plate. (Page 9, lines 10-15; Page 18, lines 5-8)

Regarding claim 21, Applicant's definition of "capillary tube" includes microfluidic systems of this type. (Specification, Page 5, lines 4-8)

Regarding claim 24, this claim includes the same limitations as claim 14, which Adourian et al anticipate, as described above. In addition, Adourian et al disclose aspirating at least two samples into at least two respective pipettes and ejecting the at least two samples into at least two respective loading wells. (Page 7, lines 5-20; Page 9, lines 10-15) The definition of "aspirate" given by the Merriam-Webster Online Dictionary is "to draw by suction", which corresponds to the pipetting action performed by the pump-driven system of Adourian et al (Page 7, lines 15-19), and is the general mode of operation used in pipetting systems.

Relevant to claims 23 and 26, Adourian et al also disclose staggered 500 micron wells on channels with 333 micron spacing (Provisional Application, Page 11, lines 7-14), and teach the advantages in cost savings and throughput gained by maximizing capillary and loading well density. (Page 4, lines 11-21)

Relevant to claim 30, Adourian et al disclose that the work surface coordinates from which the samples are transferred are sample wells in microtiter plates. (Provisional application, Page 9, lines 2-4)

Also relevant to claims 14 and 24, Adourian et al disclose having more loading wells on their electrophoresis chip than pipette tips used to load them. (Provisional

application, Page 7, lines 13-20; particularly lines 19-20 - repetition of the cycle is only necessary if not all wells are loaded in one transfer step)

Adourian et al do not explicitly address transferring the samples with a device programmed such that one-to-one correspondence between a work surface coordinate and a loading well is not required (Claims 14, 24, and 28), nor do they explicitly address decoupling the spatial arrangement of the work surface coordinates/sample wells from the capillary inlets. (Claims 23, 26, and 30)

Relevant to claims 22 and 25, Lewis discloses programmable pipetters with varying numbers of tips (e.g. Four tips are visible in the MultiPROBE system shown at the top of Page 4, Finnpipettes with variable numbers of tips discussed in the first paragraph of Page 3)

Relevant to claims 22, 23, 25, and 26, Lewis discloses variable spacing of pipette tips. (Finnpipettes at Page 3, 1st paragraph; MultiPROBE at Page 3, 9th paragraph)

Regarding claims 14 and 24, Adourian et al recite no requirement that there be a "one-to-one correspondence" between work surface coordinates and loading wells. They disclose the use of a pipetter with eight tips on fixed, 9 mm centers for sample transfer. (Page 8, lines 6-10) It would have been obvious to one having ordinary skill in the art to use arrays of more than eight loading wells (and capillaries) in a row (Suggested at Page 7, lines 13-20), given the benefits in time and labor saved through

parallel analysis. In such an array, there would obviously be no requirement for one-to-one correspondence between work surface coordinates and loading wells.

Additionally, Lewis describes pipetters with fewer pipette tips (e.g. four shown in the MultiPROBE system), and it would have been obvious to one having ordinary skill in the art at the time the invention was made to use any such pipetter within the method of Adourian et al, because the suitability of all such pipetters in facilitating fluid transfer is common knowledge within the art. Added motivation to use the MultiPROBE system lies in its variable tip spacing, which one having ordinary skill in the art would have recognized as providing highly desirable flexibility in operation.

One having ordinary skill in the art would have recognized that the use of a four channel pipetter to load an array of eight (or more) wells requires no one-to-one correspondence, since any four consecutive wells could be loaded in any one pipetting step. Additionally, the MultiPROBE system shown by Lewis has variable tip spacing (Page 3, 9th paragraph), which would obviously provide even greater flexibility in selecting which sample is loaded in which well, and would also in itself meet the limitation that "one-to-one correspondence between a work surface coordinate and a loading well is not required".

Regarding claims 23 and 26, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Adourian et al by maximizing the density of channels and loading wells on the electrophoresis chip, without considering matching the well spacing to standard microtiter plates, and using a pipetter with variable tip spacing for loading, such as the

MicroPROBE described by Lewis, because Adourian et al teach the benefits of maximizing channel density in electrophoresis chips, in increased throughput and cost reduction. (Page 4, lines 11-21) Use of a pipetter with variable tip spacing eliminates any requirement for well spacing in the chip to be coupled to the spacing of a standard microtiter plate, and greater channel and well density (with corresponding increased throughput) would obviously be attainable if the constraint of having the loading wells be spaced at an integral fraction of 9 mm was thus removed.

This rejection meets the limitations of claims 28 and 30 for the same reasons given above in addressing claims 14, 23, 24, and 26.

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Lewis as applied to claim 14 above, and further in view of either Ginsberg et al or Monthony et al.

Adourian et al and Lewis disclose a method as described above in addressing claim 14.

Neither Adourian et al nor Lewis explicitly discloses controlling the humidity around the work surface in order to reduce sample evaporation.

Ginsberg et al disclose a liquid sample analysis system that includes covers (Figure 1, covers 66 and 70) that are disposed over sample and reagent wells, in order to maintain humidity in the area under the cover and prevent evaporation of the liquids held in the wells. (Column 4, lines 42-46 and 61-62)

Monthony et al disclose a sample distribution element suitable for general use in analytical procedures (Column 6, lines 27-30), which includes a lid that "[forms] a humidity control system for restricting evaporation from the device." (Column 8, lines 13-31)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Adourian et al by controlling the humidity around the work surface to prevent sample evaporation by covering the work surface, as taught by either Ginsberg et al or Monthony et al, because one having ordinary skill in the art would have recognized that solvent evaporation would lead to unreliable results, and would have therefore been motivated to use such known methods of evaporation prevention.

12. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Lewis as applied to claim 14 above, and further in view of Truchaud et al.

Adourian et al and Lewis disclose a method as described above in addressing claim 14.

Neither Adourian et al nor Lewis explicitly discloses controlling the humidity around the work surface in order to reduce sample evaporation, or cooling the temperature of the work surface.

Truchaud et al disclose the benefits of temperature and humidity control in clinical analytical laboratories, in reduction of interference by environmental factors. (Page 1712, Advanced technologies section, 3rd paragraph)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Adourian et al by controlling the temperature and humidity of the laboratory (and therefore, the work surface and area surrounding it), as taught by Truchaud et al, because Truchaud et al teach its value in increasing the reliability of results in an analytical laboratory.

Relevant to claim 18, although Truchaud et al do not explicitly discuss reducing sample evaporation, such humidity control would necessarily and obviously include increasing the humidity of the laboratory air when a decrease in humidity is observed, in order to maintain consistent conditions. Any such humidity increase would reduce the rate of sample evaporation, thus meeting this claim limitation.

13. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Lewis as applied to claim 14 above, and further in view of Hansen et al.

Adourian et al and Lewis disclose a method as described above in addressing claim 14.

Neither Adourian et al nor Lewis explicitly discloses controlling the humidity around the work surface in order to reduce sample evaporation.

Hansen et al disclose a thermal cycling system that includes a heated cover that is disposed over sample wells that maintains humidity in the area under the cover and reduces evaporation of the liquids held in the wells. (Column 5, lines 20-30)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Adourian et al by controlling the humidity around the work surface to prevent sample evaporation by covering the work surface, as taught by Hansen et al, because one having ordinary skill in the art would have recognized that solvent evaporation would lead to unreliable results, and would have therefore been motivated to use such known methods of evaporation prevention.

Response to Arguments

14. Applicant's arguments filed 5 October 2005 have been fully considered but they are not persuasive.

Applicant argues that the provisional application to which Adourian et al claimed priority does not teach the aspects of the patent to Adourian et al used against the claims. This is not the case, as all citations to Adourian et al that are given in the rejections above are specifically to this provisional application. Applicant has failed to provide any convincing arguments that could disqualify this reference as prior art.

Applicant argues that the Examiner's citation to Page 19, lines 17-18 does not disclose "simultaneously transferring", but Applicant does not explicitly address the disclosure of the additional citation that was given, to page 6, line 20- page 7, line 20, which unambiguously discloses precisely this step. This section reads in part:

> "The robotics and associated optics serve to align and position the tip array over an industry-standard multiple-well microtitre plate and collect the desired amount of liquid sample. The motion system then lifts the tip array to the ME device, aligns to the ME device using the robotic optics system described above, and instructs the high-precision pumps to dispense the samples from the tip array into the appropriate microfabricated injection ports . . . on the ME device."

This clearly meets the limitation.

Applicant also argues that the passages cited as disclosing samples at coordinates of a work surface do not disclose this aspect of the claims. The rejection cited Page 18, lines 1-15 of the provisional application, which shows sample preparation in a 96 well microtiter plate, which are subsequently analyzed. Page 9, lines 10-15 discloses removal of samples from a microtiter plate for placement in injection ports of the electrophoresis chips. The Examiner considers samples in wells of a standard microtiter plate to clearly anticipate claims to samples located at coordinates of a work surface. Unsubstantiated assertions to the contrary are not persuasive.

Applicant also argues that there is no capillary positioned in a well in Figures 1A and 8A of the provisional application. The Examiner considers capillary 2 positioned in well 1 in Figure 8A to meet this limitation, given any reasonably broad interpretation of the claim. No convincing argument is presented to the contrary. Furthermore, since the well and capillary are formed in the same plate, and no change in their positions relative to each other is possible, this also clearly meets the limitation to a "fixedly" positioned capillary.

Applicant's arguments concerning the rejections based on Kambara et al and Briggs et al were persuasive, due to the incorporation of the limitations of claim 22 into claim 14. These rejections have been withdrawn.

Regarding the relevance of Truchaud to claim 18, Applicant argues that it is a "stretch" to argue that control of temperature or humidity in a laboratory renders obvious controlling the humidity of the environment around a work surface. The Examiner respectfully disagrees. The air in a laboratory surrounds the work surface in question, and the claimed control would be present in the combination described in the rejection. If Applicant desires a narrower reading, narrower limitations must be present. As to the assertion that no motivation for the combination is given, the Examiner redirects the Applicant to the motivation statement clearly given in the rejection.

For at least the above reasons, Applicants arguments are not persuasive.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
16 December 2005

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